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The role of interleukin 4 and IL-4RA in intervertebral disc degeneration: investigation of single nucleotide polymorphisms in genes and a systematic review & meta-analysis of IL-4 expression level

Sara Hanaei[a,b,c], Sina Abdollahzade[d], Maryam Sadr[a], Mohammad Hossein Mirbolouk[e], Ehsan Fattahi[e], Alireza Khoshnevisan[e], Nima Rezaei[b,c,f]

[a]Molecular Immunology Research Center, Tehran University of Medical Sciences, Tehran, Iran

[b]Research Center for Immunodeficiencies, Children's Medical Center, Tehran University of Medical Sciences, Tehran, Iran

[c]Network of Immunity in Infection, Malignancy and Autoimmunity (NIIMA), Universal Scientific Education and Research Network (USERN), Tehran, Iran

[d]Division of Neurosurgery, Department of Surgery, Rajayi Hospital, Qazvin University of Medical Sciences, Qazvin, Iran

[e]Department of Neurosurgery, Shariati Hospital, Tehran University of Medical Sciences, Tehran, Iran

[f]Department of Immunology, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran

Corresponding author: Nima Rezaei, Research Center for Immunodeficiencies, Children's Medical Center, Tehran University of Medical Sciences, Dr Qarib St, Keshavarz Blvd, Tehran, Iran; email: rezaei_nima@tums.ac.ir

Abstract

Background: Intervertebral disc degeneration (IVDD) is a multifactorial disease that is sensitive to the balance between anti-inflammatory and pro-inflammatory cytokines. This study investigated the single nucleotide polymorphisms (SNPs) of interleukin 4 (IL-4) in IVDD. Methods: Genomic DNA of peripheral mononuclear cells of 76 IVDD patients and 140 healthy controls were investigated for three SNPs of IL-4 (rs2243248 (−1098G/T), rs2243250 (−590 C/T), rs2070874 (−33 C/T)) and 1 SNP of IL-4RA (rs180275, +1902 A/G) through PCR-SSP method. Results: The 'C' allele frequency of IL-4 rs2243250 was 104 in 76 patients, while it was 149 in 140 controls (OR = 2, p =.001); also this SNP was significantly associated with post-operative pain reduction. The 'C' allele of IL-4 rs2070874 (130 in 76 patients, and 200 in 140 controls, OR = 2.66), and the 'CC' genotype were more frequent among patients (OR = 3.98, p <.001) than controls. 'TTT' haplotype was more common in controls (OR = 0.36, p <.001) and 'TCC' was also more common in patients (OR = 1.75, p =.012). A meta-analysis of previous studies found significantly higher IL-4 levels in disc tissues of IVDD patients, which was not similarly found in blood samples. Conclusion: The immune system plays an important role in IVDD. The extent and progress of the disease vary significantly with IL-4 level. Meanwhile, the rs2070874 and rs2243250 SNPs of IL-4 were significantly associated with IVDD in Iranian patients.

Keywords: Intervertebral disc degeneration, single nucleotide polymorphism, interleukin 4, Interleukin-4 receptor alpha, immunogenetics, cytokine